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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| 09/695,065 | 10/25/00 | BRASCH | M 0942.5000001 |

HM12/0717
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| EXAMINER | |
|---|---|
| LU,F | |
| **ART UNIT** | **PAPER NUMBER** |
| 1655 | 8 |

**DATE MAILED:** 07/17/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. 09/695,065 | Applicant(s) BIRASCH ET AL. | |
|---|---|---|---|
| | Examiner Frank W Lu | Art Unit 1655 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *6/21/2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *1-13, 21-26, 28, and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-20 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

## DETAILED ACTION

### *Election/Restriction*

1. Applicant's election of Group V, claims 14-20 and 27 in Paper No. 6 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

### *Priority*

2. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). Note that the first sentence of the specification contains a lot of related applications, it is unclear what is the relationship among this instant application and these related applications. For example, which application is the proirity document of this instant application?

### *Drawings*

3. The formal drawings submitted on February 13, 2001 have been approved by the office.

### *Claim Rejections - 35 U.S.C. § 102*

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 14-20 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Stemmer et al., (US Patent No. 5,605,793, published by February 25, 1997).

Stemmer teaches method for *in vitro* recombination which can be used in many different genes encoded proteins. One aspect of this invention provided a method for introducing one or more mutations into a template double-stranded polynucleotide, wherein the template double-stranded polynucleotide had been cleaved into random fragments of a desired size, by adding to the resultant population of double-stranded fragments one or more single or double-stranded oligonucleotides, wherein said oligonucleotides comprised an area of identity and an area of heterology to the template polynucleotide; denaturing the resultant mixture of double-stranded random fragments and oligonucleotides into single-stranded fragments, incubating the resultant population of single-stranded fragments with a polymerase under conditions which resulted in the annealing of said single-stranded fragments at regions of identity between the single-stranded fragments and formation of a mutagenized double-stranded polynucleotide; and repeating the above steps as desired (column 3, second paragraph). Either synthetic or natural single-stranded or double stranded nucleic acid fragments could be added to the random double-stranded nucleic acid fragments in order to increase the heterogeneity of the mixture of nucleic acid fragments (see column 7). In example 1, the substrate for the reassembly reaction was the dsDNA PCR product of the wild-type LacZ alpha gene from pUC18 (see claims 15 and 27) (FIG. 2). About 5 µg of the DNA substrate was digested with DNaseI. The 10-70 bp fragments were purified and were used for DNA reassembly by PCR in the absence of primer. The

product of DNA reassembly could be further amplified by PCR with primers. Finally, the PCR product was digested with restriction enzymes BamHI and Eco0109 and the reassembled fragments were ligated into a suitable vector (see columns 11 and 12). Note that: (1) any 10-70 bp fragment that were inside PCR product could be considered as an integration sequence as described in claims 14 and 16; (2) dsDNA PCR product of the wild-type LacZ alpha gene could be considered as a nucleic acid molecule flanked by recombination sites as described in claim 14 or comprising at least a first and a second recombination sites as described in claim 16 wherein BamHI and Eco0109 cloning sites could be considered as first and a second recombination sites and were separated by at least a portion of said nucleic acid molecule as described in claim 16 and 18; (3) the vector containing dsDNA PCR product of the wild-type LacZ alpha gene was a circular molecule as described in claim 17; and (4) although Stemmer did not show that 10-70 bp fragments (see above) comprised selectable markers as described in claim 20, in the absence of convincing evidence to the contrary, these limitations is considered to be inherent to the reference taught by Stemmer since these fragments could bind T4 polynucleotide kinase (a product that modify a substrate, see the specification, page 27) and labeled $P^{32}$ in the 5' end of this fragments.

Therefore, Stemmer teaches all limitations recited by claims 14-20 and 27.

6. Claims 16-20 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Atlung *et al.*, (Gene 107, 11-7, October 1991).

Atlung *et al.*, teach a versatile method for integration of modified genes and gene fusions into the bacteriophage lambda attachment site (attB) of the Escherichia coli chromosome. As

shown in Figure 2, the method use two components to perform the recomination: (1) a DNA integration cassette, flanked by multiple restriction enzyme sites, which contained the lambda attP site and, as a selectable marker, the Tn5 aphA gene conferring kanamycin resistance ($Km^R$); and (2) a plasmid with the lambda int gene transcribed from the tet promoter. A fragment carrying the gene in question was ligated to the integration cassette, resulting in a circular piece of DNA unable to replicate. The ligation product was then transformed into a strain that contains the int-carrying plasmid. Selection for $Km^R$ resulted in colonies with the cassette integrated into the attB site of the E. coli chromosome (see abstract in page 11 and 14). Note that ligation sites could be considered as first and second recombination sites as described in claim 16.

Therefore, Atlung *et al.*, teach all limitations recited by claims 16-20 and 27.

***Conclusion***

7. No claim is allowed.

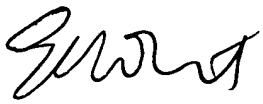
8. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
July 13, 2001



Ethan Whisenant, Ph.D.
Primary Examiner (FSA)